

Art Unit: 1654

**DETAILED ACTION*****Election/Restrictions***

Applicant's election with traverse of group I claims (25-42 and 44) and election of polymerisable lipids as species of lipids; oligopeptide sequence as species of ligands; vitamins as species of active substance; amino acids as species of spacer unit and diacetylene lipids as species of polymerizable group in the reply filed on 9/7/10 is acknowledged. Mr. Ed Freedman was contacted by telephone on 10/14/10 to obtain further clarity on the election of species as the elected species represented genera of different species. Mr. Freedman elected phospholipids as species of lipids; SEQ ID NO: 1 as species of ligands and D-alpha-tocopherol as species of active substance. The traversal is on the ground(s) that there is unity of invention in the instant application and the applied prior art show lack of unity in the instant application does not recite that the polymerizable group is added on the non-polar hydrocarbon chain of lipid molecule. This is not found persuasive because the use of incorporation of polymerizable groups in the hydrophobic chain of a lipid in a liposome is well known in the art as illustrated in Brey (US 2002/00418861 A1).

The requirement is still deemed proper and is therefore made FINAL.

***Specification***

The abstract of the disclosure is objected to because the abstract refers to Figure 3. The numbers disclosed in the abstract text (probably) corresponds to the numbers associated within the figure 3. However, the number (5) that corresponds to the ligand being peptide is not part of the figure 3. Correction is required. See MPEP § 608.01(b).

Art Unit: 1654

2. The specification of the instant application also lacks the required format for presentation as provided in 37 CFR 1.77(b). The instant specification does not conform to the guidelines with sections under different titles such as:

(b) Cross-reference to related applications,

(f) Background of the invention.

(1) Field of the invention.

(2) Description of related art including information disclosed under 37 CFR 1.97 and 1.98.

(g) Brief summary of the invention, etc.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

### **Arrangement of the Specification**

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.

(b) CROSS-REFERENCE TO RELATED APPLICATIONS.

(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.

(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.

(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.

(f) BACKGROUND OF THE INVENTION.

(1) Field of the Invention.

(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(g) BRIEF SUMMARY OF THE INVENTION.

(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).

Art Unit: 1654

- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

3. The disclosure is objected to because of the following informalities: There is a space between letters 'b' and 'e' on page 4, paragraph 6 and line 2.

Appropriate correction is required.

*Status of the pending claims*

Applicant's amendment to claims in the response filed on 9/7/10 has been acknowledged.

Claims 25-47 are pending.

Claim 43 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/7/10.

Claims 45-47 are use claims and are non-statutory.

Claims 33, 39-42 as being withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made with traverse in the reply filed on 9/7/10.

A search for the applicant's election of SEQ ID NO: 1 indicated that SEQ ID NO: 1 and alpha-tocopherol are not free of prior art. The prior art found has been applied in the rejection set forth below.

Claims 25-32, 34-38 and 44 are examined on the merit.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-32, 34-38 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims as recited leads to multiple interpretations: a) as presented the claim recite that “it is transport system for ‘substances’ containing hybrid particles comprising...”. The nature of the substance being transported is not evident from the claim or b) “is it a transport system containing hybrid particles comprising...”. It is unclear from the claims as recited whether the claims are reciting one of the two aforementioned interpretations or both.

2. It is unclear from the claim as recited the significance of numbers recited in the claims within parenthesis, i.e., (2), (3), (5), etc. It is unclear whether numbers corresponds to a figure in the instant application. MPEP 2173.05(S) states that “[W]here possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table “is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant’s convenience.” Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted). Reference characters corresponding to elements recited in the detailed description and

Art Unit: 1654

the drawings may be used in conjunction with the recitation of the same element or group of elements in the claims. See MPEP § 608.01(m)".

3. Regarding claims 27 and 28, the phrase "for example" (on line 4) renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

4. Regarding claims 27, 28, 34 and 36, the phrase "etc." (on line 5) renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

5. Claims 27 and 28, each contains two periods at the end of the claim. MPEP section 608.01(m) [R-7] states that, "[E]ach claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations".

6. Regarding claim 27 and 28, the phrase "such as" (on line 4) renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

7. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. The instant claim 25 is indefinite as it recites a

Art Unit: 1654

transport system for substances containing hybrid particles. The claim also recites that the hybrid particles comprises a ligand which is a peptide that has specific sequence for selective transport purposes and 'selectively transported liposome transport at least one micronutrient'. It is unclear from the claim as presented whether the liposome of the instant invention already transported the micronutrient or it is used for transporting micronutrient.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25-29, 31, 34-36 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Brey (US 2002/0041861).

In the instant invention applicants claim a transport system for substances containing hybrid particles comprising at least one layer of lipid molecules, at least one spacer unit bonded ligand, which ligand is a peptide which has a specific sequence for selective transport purposes and the selectively transported liposomes transport at least one micronutrient wherein at least one polymerizable group is incorporated in the hydrocarbon chain of the lipid molecule.

Brey discloses a novel drug delivery system that delivers biologically active substances utilizing novel polymerized liposomes made of polymerizable fatty acid having a polymerizable functional group, a surfactant, optionally coupled to ligands that targets mucosal tissues (Abstract). The novel polymerizable fatty acid has the formula  $R_4-X-PEG-Y-B$ , wherein  $R_4$  is

Art Unit: 1654

the polymerizable group is a lipophilic chain (fatty acid chain) with at least one polymerizable group that enable polymerization, X and Y are functional linkage moiety such as an ester, amide or a carbamate and B is a ligand (page 4, [0050-0051]. The polymerizable moieties on the fatty acids copolymerize with polymerizable phospholipids in a polymerizable liposome the functional acid group of the fatty acids are derivatized with targeting ligands [0052]. The ligands that can be attached are peptides, proteins, lectins, insulin, antibiotics, hormones, vaccines, etc., [0088-0090]. This reads on the instant claims 25, 26, 28, 29, 31 and 34-36. Brey also discloses that the targeted polymerized liposomes are used as the carriers in a drug delivery system [0086-0088]. This reads on the instant claim 44. Brey further discloses that the polymerizable moiety in the hydrophobic region of the fatty acid is selected from a group consisting of a diene, diacetylene, methacrylate and a thiol group. This reads on the instantly elected species of polymerizable group which is diacetylene lipids.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

Art Unit: 1654

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25-32, 34-38 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brey (US 2002/0041861) in view of Unger (US 6,120,751).

In the instant invention applicants claim a transport system for substances containing hybrid particles comprising at least one layer of lipid molecules, at least one spacer unit bonded ligand, which ligand is a peptide which has a specific sequence for selective transport purposes and the selectively transported liposomes transport at least one micronutrient wherein at least one polymerizable group is incorporated in the hydrocarbon chain of the lipid molecule.

Brey discloses a novel drug delivery system that delivers biologically active substances utilizing novel polymerized liposomes made of polymerizable fatty acid having a polymerizable functional group, a surfactant, optionally coupled to ligands that targets mucosal tissues (Abstract). The novel polymerizable fatty acid has the formula  $R_4-X-PEG-Y-B$ , wherein  $R_4$  is the polymerizable group is a lipophilic chain (fatty acid chain) with at least one polymerizable group that enable polymerization, X and Y are functional linkage moiety such as an ester, amide or a carbamate and B is a ligand (page 4, [0050-0051]). The polymerizable moieties on the fatty acids copolymerize with polymerizable phospholipids in a polymerizable liposome the functional acid group of the fatty acids are derivatized with targeting ligands [0052]. The ligands that can be attached are peptides, proteins, lectins, insulin, antibiotics, hormones, vaccines, etc., [0088-0090]. This reads on the instant claims 25, 26, 28, 29, 31 and 34-36. Brey also discloses that the

Art Unit: 1654

targeted polymerized liposomes are used as the carriers in a drug delivery system [0086-0088].

This reads on the instant claim 44. Brey further discloses that the polymerizable moiety in the hydrophobic region of the fatty acid is selected from a group consisting of a diene, diacetylene, methacrylate and a thiol group. This reads on the instantly elected species of polymerizable group which is diacetylene lipids.

Although, Brey discloses that the ligands attached to the polymerizable lipids used in the formation of liposomes for delivery of active ingredients can be peptides, hormones and lectins. It does not specifically disclose the instantly elected species of the peptide GRGDSP (SEQ ID NO: 1).

Unger discloses liposomes made of polymerizable lipids (column 21 and 22) with targeting ligands that include instantly claimed SEQ ID NO: 1, i.e., GRGDSP (column 49, line 30). Unger discloses many other peptides that targets additional receptors as disclosed in column 49 and 50. This reads on the instant claims 25 and 29-32. Unger also discloses the instantly claimed tocopherol as the species of the vitamin (column 20, line 3).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Brey and Unger to arrive at the instant invention, because, Brey discloses the conjugation of peptides to the polymerizable fatty acids in the preparation of liposomes as transport systems and Unger discloses specific ligands such as instantly claimed GRGDSP (SEQ ID NO: 1) for targeted delivery to specific receptors on the cell surface. One of the ordinary skill in the art would have been motivated to do so because, Unger clearly states that "A wide variety of targeting ligands may be employed to direct the composition (liposome comprising the active ingredient) to receptors (GPIIbIIIa) (column 49, lines 23-25). A reference is good not only for

Art Unit: 1654

what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the foregoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1654

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SATYANARAYANA R. GUDIBANDE/  
Examiner, Art Unit 1654

/Andrew D Kosar/  
Primary Examiner, Art Unit 1654